CLAIMS

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a polynucleotide fragment of SEQ ID NO:1 or a polynucleotide fragment of the cDNA sequence included in ATCC deposit No:PTA-2766, which is hybridizable to SEQ ID NO:1;

(b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:2 or a polypeptide fragment encoded by the cDNA sequence included in ATCC deposit No:PTA-2766, which is hybridizable to SEQ ID NO:1;

(c) a polynucleotide encoding a polypeptide domain of SEQ ID NO:2 or a polypeptide domain encoded by the cDNA sequence included in ATCC deposit No:PTA-2766, which is hybridizable to SEQ ID NO:1;

(d) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:2 or a polypeptide epitope encoded by the cDNA sequence included in ATCC deposit No:PTA-2766, which is hybridizable to SEQ ID NO:1;

(e) a polynucleotide encoding a polypeptide of SEQ ID NO:2 or the cDNA sequence included in ATCC deposit No:PTA-2766, which is hybridizable to SEQ ID NO:1, having biological activity;

(f) a polynucleotide which is a variant of SEQ ID NO:1;

(g) a polynucleotide which is an allelic variant of SEQ ID NO:1;

(h) a polynucleotide which encodes a species homologue of SEQ ID NO:2;

(i) a polynucleotide encoding a polypeptide of SEQ ID NO:2;

(j) a polynucleotide comprising nucleotides 182 to 1372 of SEQ ID NO:1, wherein said nucleotides encodes the mature polypeptide of SEQ ID NO:2;

(k) a polynucleotide comprising nucleotides 71 to 1372 of SEQ ID NO:1, wherein said nucleotides encode a polypeptide of SEQ ID NO:2 minus the start codon;

(l) a polynucleotide comprising nucleotides 68 to 1372 of SEQ ID NO:1, wherein said nucleotides encode a polypeptide of SEQ ID NO:2 including the start codon;

(m) a polynucleotide which represents the complimentary sequence (antisense) of any one of (a) thru (l) above; and

(n) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(m), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.

2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a serpin protein.

3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:2 or the polypeptide encoded by the cDNA sequence included in ATCC deposit No:PTA-2766, which is hybridizable to SEQ ID NO:1.

4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:1 or the cDNA sequence included in ATCC deposit No:PTA-2766, which is hybridizable to SEQ ID NO:1.

5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.

8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.

9. A recombinant host cell produced by the method of claim 8.

10. The recombinant host cell of claim 9 comprising vector sequences.

11. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a polypeptide fragment of SEQ ID NO:2 or the encoded sequence included in ATCC deposit No:PTA-2766;

(b) a polypeptide fragment of SEQ ID NO:2 or the encoded sequence included in ATCC deposit No:PTA-2766, having biological activity;

(c) a polypeptide domain of SEQ ID NO:2 or the encoded sequence included in ATCC deposit No:PTA-2766;

(d) a polypeptide epitope of SEQ ID NO:2 or the encoded sequence included in ATCC deposit No:PTA-2766;

(e) a full length protein of SEQ ID NO:2 or the encoded sequence included in ATCC deposit No:PTA-2766;

(f) a variant of SEQ ID NO:2;

(g) an allelic variant of SEQ ID NO:2;

(h) a species homologue of SEQ ID NO:2;

(i) a polypeptide comprising amino acids 39 to 435 of SEQ ID NO:2, wherein said amino acids 39 to 435 comprise the mature polypeptide of SEQ ID NO:2;

(j) a polypeptide comprising amino acids 2 to 435 of SEQ ID NO:2, wherein said amino acids 2 to 435 comprise a polypeptide of SEQ ID NO:2 minus the start methionine;

(k) a polypeptide comprising amino acids 1 to 435 of SEQ ID NO:2; and

(l) a polypeptide encoded by the cDNA contained in ATCC Deposit No. PTA-2766.

12. The isolated polypeptide of claim 11, wherein the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus.

13. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.

14. A recombinant host cell that expresses the isolated polypeptide of claim 11.

15. A method of making an isolated polypeptide comprising:

(a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed; and

(b) recovering said polypeptide.

16. The polypeptide produced by claim 15.

17. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polynucleotide of claim 1.

18. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.

19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:

(a) contacting the polypeptide of claim 11 with a binding partner; and

(b) determining whether the binding partner effects an activity of the polypeptide.

21. The gene corresponding to the cDNA sequence of SEQ ID NO:2.

22. A method of identifying an activity in a biological assay, wherein the method comprises:

(a) expressing SEQ ID NO:1 in a cell;

(b) isolating the supernatant;

(c) detecting an activity in a biological assay; and

(d) identifying the protein in the supernatant having the activity.

23. The product produced by the method of claim 20.

24. A process for making polynucleotide sequences encoding gene products having altered serpin activity comprising,

a) shuffling a nucleotide sequence of claim 1,

b) expressing the resulting shuffled nucleotide sequences and,

c) selecting for altered serpin activity compared to the activity of the gene product of said unmodified nucleotide sequence.

25) A shuffled polynucleotide sequence produced from the process of claim 24.

26) The method for preventing, treating, or ameliorating a medical condition of claim 17, wherein the medical condition is a cardiovascular condition.

27) The method for preventing, treating, or ameliorating a medical condition of claim 17, wherein the medical condition is an inflammatory disease.

28) The method for preventing, treating, or ameliorating a medical condition of claim 27, wherein the medical condition is an inflammatory disease where proteases, either directly or indirectly, are involved in disease progression.

29) The method for preventing, treating, or ameliorating a medical condition of claim 17, wherein the medical condition is a cancer.

30) The method for preventing, treating, or ameliorating a medical condition of claim 17, wherein the medical condition is a blood disorder.

31) A computer for producing a three-dimensional representation of a molecule or molecular complex, wherein said molecule or molecular

complex comprises the structural coorrdinates of the model LSI-01 in accordance with Table III, or a three-dimensional representation of a homologue of said molecule or molecular complex, wherein said homologue comprises backbone atoms that have a root mean square deviation from the backbone atoms of not more than 4.0 .ANG. wherein said computer comprises:

A.) A machine-readable data storage medium, comprising a data storage material encoded with machine readable data, wherein the data is defined by the set of structure coordinates of the model LSI-01 according to Table III, or a homologue of said model, wherein said homologue comprises backbone atoms that have a root mean square deviation from the backbone atoms of not more than 4.0Å;

B.) a working memory for storing instructions for processing said machine-readable data;

C.) a central-processing unit coupled to said working memory and to said machine-readable data storage medium for processing said machine readable data into said three-dimensional representation; and

D.) a display coupled to said central-processing unit for displaying said three-dimensional representation.

32) The computer according to claim 31 wherein the machine-readable data storage medium, wherein said machine readable data storage medium is defined by the set of structure coordinates of the model for LSI-01 according to Table III, or a homologue of said molecule, said homologue having a root mean square deviation from the backbone atoms of not more than 3.0 Å.

33) A model comprising all or any part of the model defined by structure coordinates of LSI-01 according to Table III, or a mutant or homologue of said molecule or molecular complex.

34) A method for identifying a mutant of LS1-01 with altered biological properties, function, or reactivity, the method comprising the step selected from the group consisting of:

a. Using the LSI-01 model or a homologue of said model according to Table III, for the design of protein mutants with altered biological function or properties which exhibit the therapeutic effect of claim 17 above;

b. Using the LSI-01 model or a homologue of said model, for the design of a protein with mutations in the reactive loop region comprised of the amino acids A384,T385, A386, A387, T388, T389, T390, K391, F392, I393, V394, R395, S396, K397, D398, G399, P400, S401, Y402, F403, T404 according to Table III with altered biological function or properties exhibit the therapeutic effect of claim 17 above;

c. Using the LSI-01 model or a homologue of said model, for the design of a protein with mutations in the heparin binding region comprised by the amino acids Y63-E80, E125-T140, A306-S315 according to Table III with altered biological function or properties exhibit the therapeutic effect of claim 17 above; and

d. Using the LSI-01 model or a homologue of said model, for the design of a protein with mutations cleaved reaction loop binding region comprised by the amino acids N185-T201, Q202-I209, A217-K227, K368-V377 according to Table III , with altered biological function or properties exhibit the therapeutic effect of claim 17 above.

35) A method for identifying modulators of LSI-01 biological properties, function, or reactivity, the method comprising the step selected from the group consisting of:

a.) modeling test compounds that overlay spatially into the heparin binding region defined by all or any portion of residues Y63-E80, E125-T140, A306-S315, of the three-dimensional LSI-01 structural model according to Table III, or using a homologue or portion thereof; and

b.) modeling test compounds that overlay spatially into the regions defined by all or any portion of the cleaved reactive loop binding regions comprised of by the residues N185-T201, Q202-I209, A217-K227, K368-V377 of the three-dimensional structural model according to Table III, or using a homologue or portion thereof.

36) A method for identifying structural and chemical features of LSI-01 using the structural coordinates set forth in claim 33 comprising the step selected from a member of the group consisting of:

a. employing identified structural or chemical features to design or select compounds as potential LSI-01 modulators;

b. employing the three-dimensional structural model to design or select compounds as potential LSI-01 modulators;

c. synthesizing the potential LSI-01 modulators; and

d. screening the potential LSI-01 modulators in an assay characterized by binding of a protein to the LSI-01.

37). The method according to claim 36 wherein the potential LSI-01 modulator is selected from a database.

38.) The method according to claim 36 wherein the potential LSI-01 modulator is designed de novo.

39.) The method according to claim 36 wherein the potential LSI-01 modulator is designed from a known modulator of activity.

40.) The method for preventing, treating, or ameliorating a medical condition of claim 17, wherein the medical condition is an immune disorder.

41.) The method for preventing, treating, or ameliorating a medical condition of claim 40, wherein the medical condition is a T-cell malignancy.

42.) The method for preventing, treating, or ameliorating a medical condition of claim 41, wherein the medical condition is a leukemia.

43.) The method for preventing, treating, or ameliorating a medical condition of claim 42, wherein the medical condition is a B-cell leukemia.

44.) An isolated nucleic acid molecule consisting of a polynucleotide having a nucleotide sequence selected from the group consisting of:

(a) a polynucleotide encoding a polypeptide of SEQ ID NO:2;

(b) a polynucleotide comprising nucleotides 182 to 1372 of SEQ ID NO:1, wherein said nucleotides encodes the mature polypeptide of SEQ ID NO:2;

(c) a polynucleotide comprising nucleotides 71 to 1372 of SEQ ID NO:1, wherein said nucleotides encode a polypeptide of SEQ ID NO:2 minus the start codon;

(d) a polynucleotide comprising nucleotides 68 to 1372 of SEQ ID NO:1, wherein said nucleotides encode a polypeptide of SEQ ID NO:2 including the start codon;

(e) a polynucleotide encoding the LSI-01 polypeptide encoded by the cDNA clone contained in ATCC Deposit No. PTA-2766; and

(f) a polynucleotide which represents the complimentary sequence (antisense) of any one of the (a) thru (e) above.

45. The isolated nucleic acid molecule of claim 44, wherein the polynucleotide comprises a nucleotide sequence encoding a serpin protein.

46. The isolated nucleic acid molecule of claim 44, wherein the polynucleotide comprises a nucleotide sequence encoding the polypeptide sequence identified as SEQ ID NO:2.

47. The isolated nucleic acid molecule of claim 45, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

48. A recombinant vector comprising the isolated nucleic acid molecule of claim 45.

49. A recombinant host cell comprising the recombinant vector of claim 48.

50. An isolated polypeptide consisting of an amino acid sequence selected

(a) a polypeptide fragment of SEQ ID NO:2 having serpin activity;

(b) a polypeptide domain of SEQ ID NO:2 having serpin activity;

(c) a full length protein of SEQ ID NO:2;

(d) a variant of SEQ ID NO:2 having serpin activity;

(e) a polypeptide comprising amino acids 39 to 435 of SEQ ID NO:2, wherein said amino acids 39 to 435 comprise the mature polypeptide of SEQ ID NO:2;

(e) a polypeptide comprising amino acids 2 to 435 of SEQ ID NO:2, wherein said amino acids 2 to 435 comprise a polypeptide of SEQ ID NO:2 minus the start methionine;

(f) a polypeptide comprising amino acids 1 to 435 of SEQ ID NO:2; and

(g) a polypeptide encoded by the cDNA contained in ATCC Deposit No. PTA-2766.

51.) A method of screening for candidate compounds capable of binding to and/or modulating activity of a potassium channel beta subunit, comprising:

(a.) contacting a test compound with a substantially or partially purified polypeptide according to claim 45; and

(b.) selecting as candidate compounds those test compounds that bind to and/or modulate activity of the polypeptide.

52.) The method according to claim 51, wherein the candidate compounds are small molecules.

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